**PROBLEM SOLVING AND DEMO-Rosenberg**

VAGAL STIMULATION

Ach released from post ganglionic PSNS from end of vagus nerve (PSNS)—ganglia are at the end of the long preganglionic nerve. Ach stimulates M receptors and cause a decrease in HR. As BP and HR decrease and then you turn off the stimulus you see a rise in BP because it is compensating through the SNS.

ACH-5 mg/kg

-Decreases both systolic and diastolic BP and effect is short lived because it is metabolized fast.

-Most of the affect is on Ach acting on vasculature working on M receptors to decrease SM contraction

-Lasted 15 sec

METHACHOLINE

-Longer half-life than Ach and less susceptible to AchE. So should see more intense effect.

-You see a more pronounced BP

-Lasted 2.5 min

NEOSTIGMINE

-Cholinesterase inhibitor

-Have to wait a few minutes to see the total effect

-Allows Ach to accumulate at all the synapses it is released

-Neostigmine stimulates M receptors and you see a transient decrease in BP

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NEOSTIGMINE + VAGAL STIMULATION

-Then you stimulate vagus n. to get the Ach release. —See MUCH MORE PRONOUNCED EFFECT

-Decrease in BP and in HR and then b/c BP was so low SNS kicked in and caused a slight increase in BP after

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NEOSTIGMINE + ACH

-Then give ACH and you see a very pronounced effect on BP and HR and longer lasting effect b/c the AchE is inhibited. (The breakdown we do see if due to water.

NEOSTIGMINE + METHACHOLINE

* HR slows while BP drops.
* If this was your patient what drug could you give to counteract these effects? To prevent vasodilation you give atropine (blocks muscarinic receptors in the vascular SM)

AFTER GIVEN THE ANIMAL ACHE INHIBITOR AND ATROPINE

--After vagal stimulation—no effect on HR

--B/c Ach cannot work on its M receptors in SA node to decrease HR

NEOSTIGMINE + ATROPINE + ACH

—No effect on BP or HR. Atropine has effectively blocked M receptors in VSM, SA node, and heart

NEOSTIGMINE + ATROPINE + METHACHOLINE

—No effect b/c of atropine

--Atropine is a competitive antagonist—it can be removed from receptor—or larger dose of an agonist may be able to block its activity

NEOSTIGMINE + ATROPINE + 100 times more ACH

—See increase in BP and the HR greatly

--Why did it cause so much increase in BP?

--Stimulates PSNS and SNS ganglia

--But atropine PSNS postganglionic receptors are blocked

--Only thing we see is Ach stimulation of SNS

NEOSTIGMINE + ATROPINE + HEXOMATHONIUM (ganglionic blocking agent)

--Given large dose of ACh---now we see a decrease in BP –indicating that the hexomathonium blocks SNS and the decrease in BP indicates that the competitive blocking action of atropine can be overcome by a large dose of agonist

GIVEN EPINEPHRINE—0.5 mg/kg (low dose)

--Decrease in diastolic pressure (B2 receptors on VSM and relaxation) not much change in systolic and increase in contractile force (B1 receptors in myocardium; no alpha affect)

--Alpha 1, 2, and beta 1, 2 receptors are stimulated by epinephrine

GIVEN EPINEPHRINE—1 mg/kg (higher dose)

-More pronounced effect on alpha-receptors

--Diastolic and systolic increase (stimulating alpha receptors in the periphery and causing vaso contraction) and increase in contractile force (B1 receptors in myocardium)

NOREPINEPHRINE

-Stimulates only alpha receptors in the vasculature and B1 in the heart

-Severe vasoconstriction in periphery—very high BP

-Increase in contractility in the heart—B1 effect

ISOPROTERENOL

-Stimulates only B1 and B2 receptors

-B2🡪 ↓ in diastolic

-B1--↑ in contractile force

-↑ In HR

PHENTOLAMINE (alpha blocker)

-BP have decreased b/c SNS maintain tone of BV’s through NE and alpha receptors so now NE has no effect on receptors which causes ↓ in BP

PHENTOLAMINE + NOREPINEPHRINE

-NE (alpha and B1)🡪 what you see a very slight ↓ in BP

-Due to increase in contractility

-B1 receptors are still functional but the alpha R are blocked

PHENTOLAMINE + EPINEPHRINE

-Epinephrine (alpha and beta receptors)🡪 now will only see beta effect🡪 so increase in contractile force and slight decrease in BP (both diastolic and systolic)

-Epinephrine reversal (↑ BP before alpha blocker and then ↓ BP after alpha blocker)

PHENTOLAMINE + ISO

-ISO (only Beta)🡪 so no change in response to what was seen before.

PHENTOLAMINE + PROPANOLOL (beta blocker)

--BP is the same

-Contractile force is ↓

-And HR was slower

PHENTOLAMINE + PROPANOLOL + EPI

-Very slight rise in BP (b/c EPI was able to overcome the blockade produced by phentolamine)

PHENTOLAMINE + PROPANOLOL + ISO

--ISO (just beta)🡪propranolol blocks effect of ISO